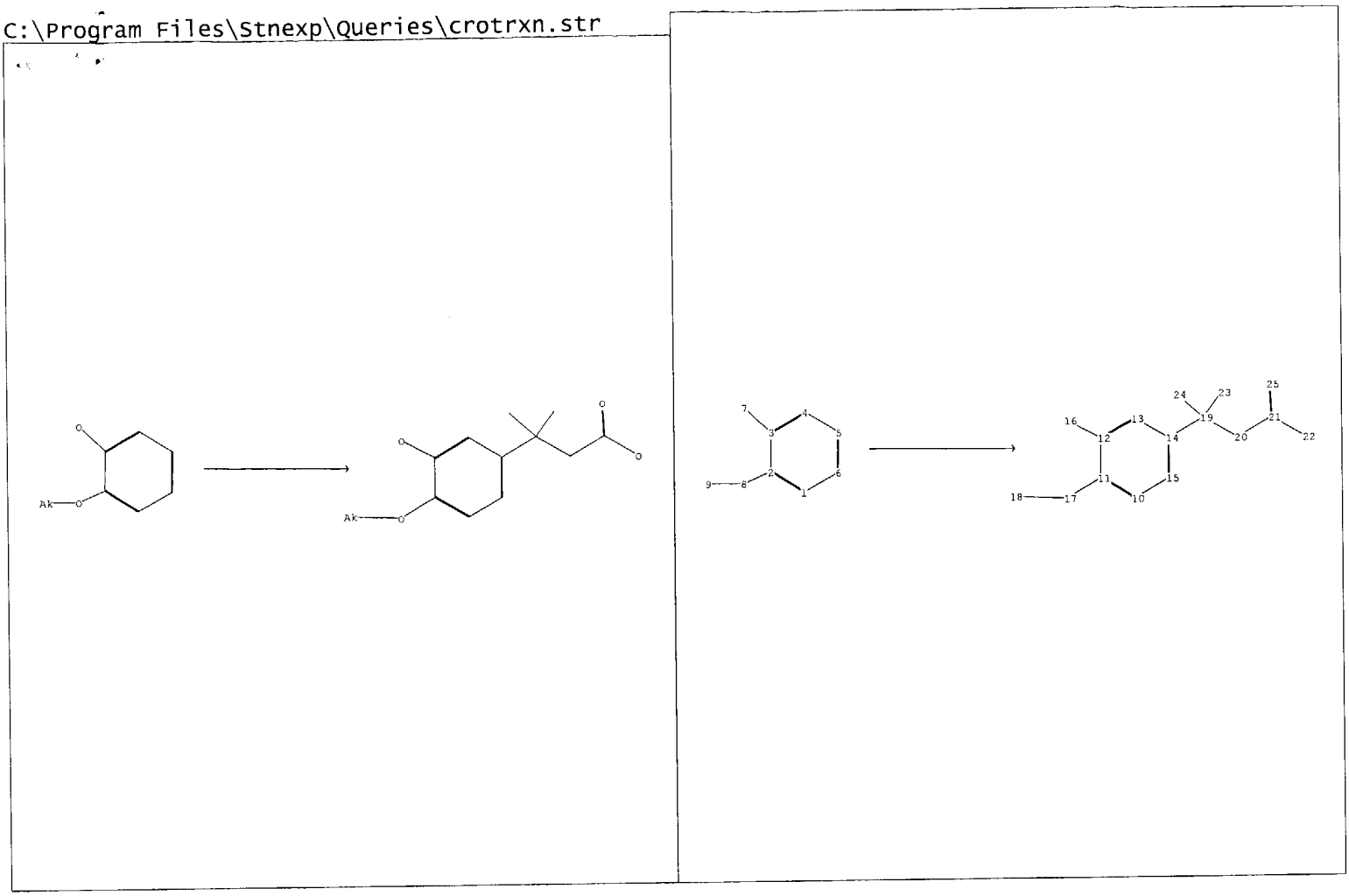
C:\Program Files\Stnexp\Queries\crotrxn.str



chain nodes :
7 8 9 16 17 18 19 20 21 22 23 24 25
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15
chain bonds :
2-8 3-7 8-9 11-17 12-16 14-19 17-18 19-20 19-23 19-24 20-21 21-22 21-25
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
2-8 3-7 8-9 11-17 12-16 17-18 21-22 21-25
exact bonds :
14-19 19-20 19-23 19-24 20-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS
fragments assigned product role:
containing 10
fragments assigned reactant/reagent role:
containing 1

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=> d his

     (FILE 'HOME' ENTERED AT 10:31:10 ON 30 JUN 2004)

     FILE 'CASREACT' ENTERED AT 10:31:21 ON 30 JUN 2004
L1                STRUCTURE UPLOADED
L2              0 S L1 SSS
L3             11 S L1 SSS FULL
L4              0 S L1

     FILE 'CAPLUS' ENTERED AT 10:34:10 ON 30 JUN 2004
L5             11 S L3

     FILE 'REGISTRY' ENTERED AT 10:34:19 ON 30 JUN 2004
L6              1 S 541-47-9/RN

     FILE 'CAPLUS' ENTERED AT 10:34:48 ON 30 JUN 2004
L7            983 S L6
L8              1 S L7 AND L5

     FILE 'REGISTRY' ENTERED AT 10:37:12 ON 30 JUN 2004

     FILE 'CAPLUS' ENTERED AT 10:37:12 ON 30 JUN 2004

     FILE 'REGISTRY' ENTERED AT 10:38:13 ON 30 JUN 2004
L9                STRUCTURE UPLOADED
L10             1 S L9 SSS
L11            48 S L9 SSS FULL
L12               STRUCTURE UPLOADED
L13            50 S L12 SSS
L14        281769 S L12 SSS FULL

     FILE 'CAPLUS' ENTERED AT 10:39:51 ON 30 JUN 2004
L15             0 S L11 AND L14 AND L6
L16            33 S L11/PREP
L17             1 S L16 AND L14
L18             0 S L17 AND L6

     FILE 'REGISTRY' ENTERED AT 10:46:32 ON 30 JUN 2004

     FILE 'CAPLUS' ENTERED AT 10:46:33 ON 30 JUN 2004

     FILE 'CASREACT' ENTERED AT 10:47:17 ON 30 JUN 2004

     FILE 'CAPLUS' ENTERED AT 10:47:21 ON 30 JUN 2004

     FILE 'CASREACT' ENTERED AT 10:50:58 ON 30 JUN 2004

     FILE 'CAPLUS' ENTERED AT 10:51:02 ON 30 JUN 2004

=> d l1
L1 HAS NO ANSWERS
L1                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> d l6
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:Y
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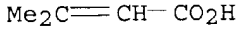
L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **541-47-9** REGISTRY
CN 2-Butenoic acid, 3-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Crotonic acid, 3-methyl- (8CI)
OTHER NAMES:
CN β,β-Dimethylacrylic acid
CN β-Methylcrotonic acid
CN 3,3-Dimethylacrylic acid
CN 3-Methyl-2-butenoic acid
CN 3-Methylcrotonic acid
CN NSC 2549
CN NSC 97179
CN Senecioic acid
FS 3D CONCORD
MF C5 H8 O2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, NAPRALERT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

978 REFERENCES IN FILE CA (1907 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
983 REFERENCES IN FILE CAPLUS (1907 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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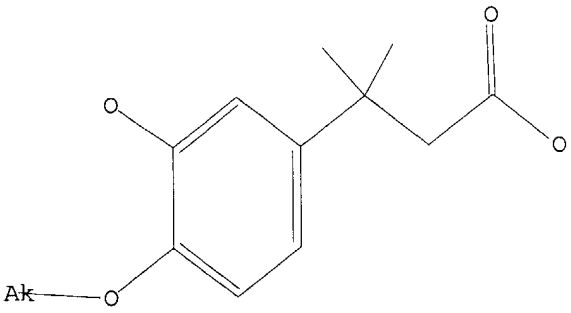
L9 STR



Structure attributes must be viewed using STN Express query preparation.

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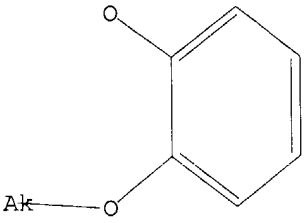
L12 STR



Structure attributes must be viewed using STN Express query preparation.

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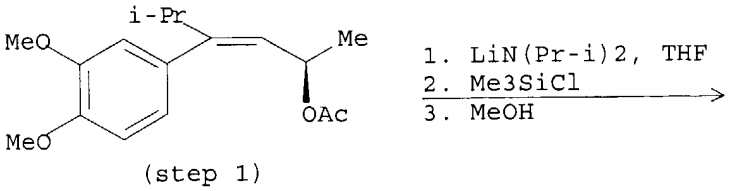
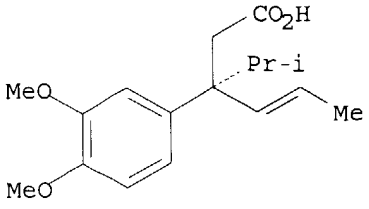
L3 ANSWER 1 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

RX(12) OF 565



(step 1)

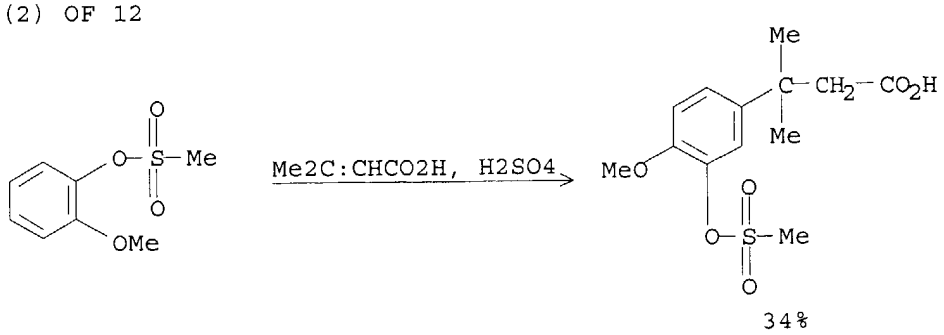


63%

REF: European Journal of Organic Chemistry, (7), 1349-1357; 2001
NOTE: stereoselective

L3 ANSWER 2 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

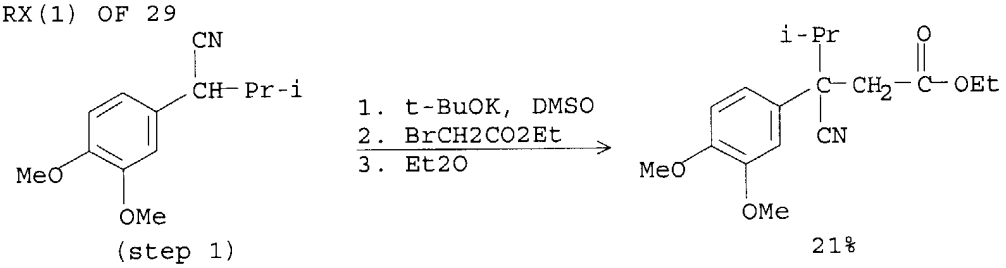
RX(2) OF 12



REF: PCT Int. Appl., 2001038297, 31 May 2001
NOTE: 70.degree. for 12 h

L3 ANSWER 3 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

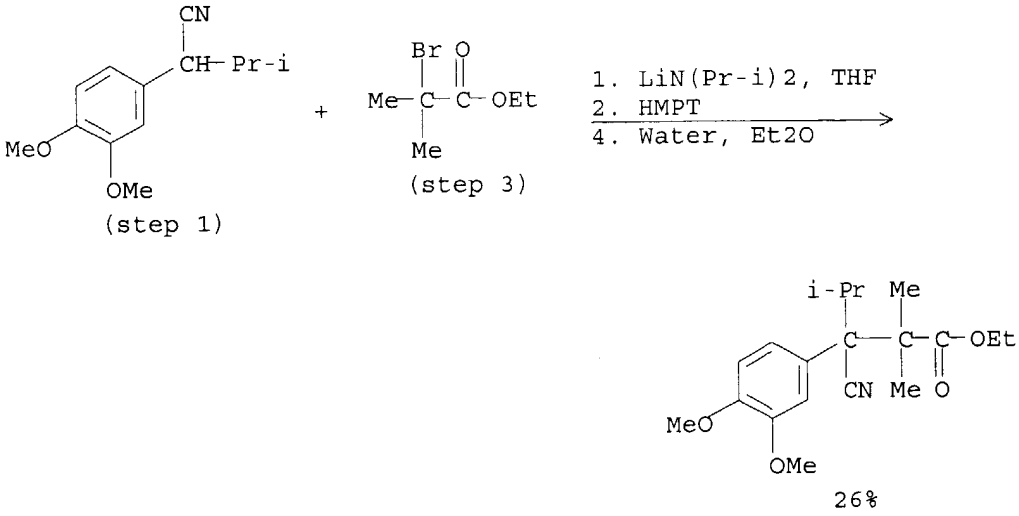
RX(1) OF 29



REF: Archiv der Pharmazie (Weinheim, Germany), 333(10), 329-336; 2000

L3 ANSWER 4 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

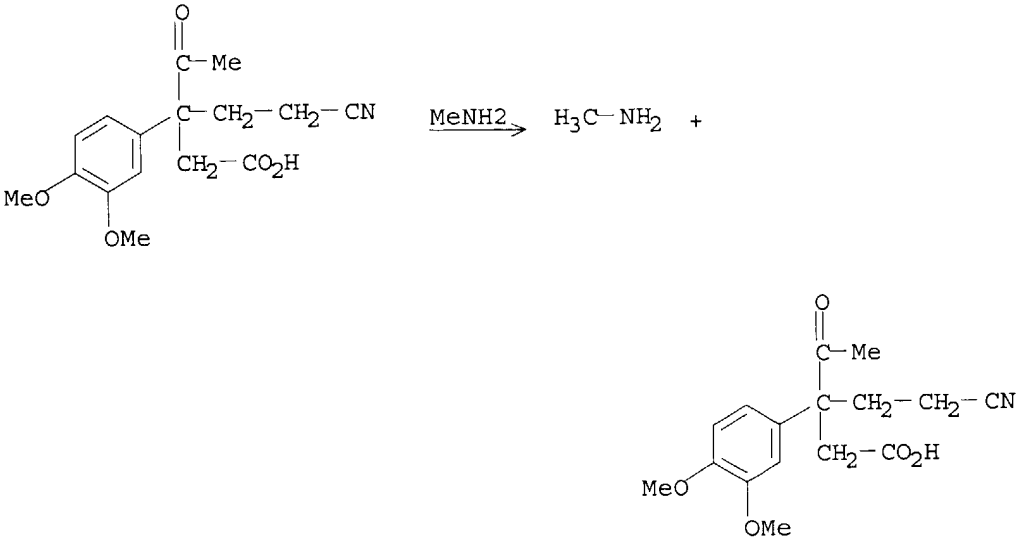
RX(1) OF 1



REF: European Journal of Organic Chemistry, (11), 3179-3183; 1999

L3 ANSWER 5 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

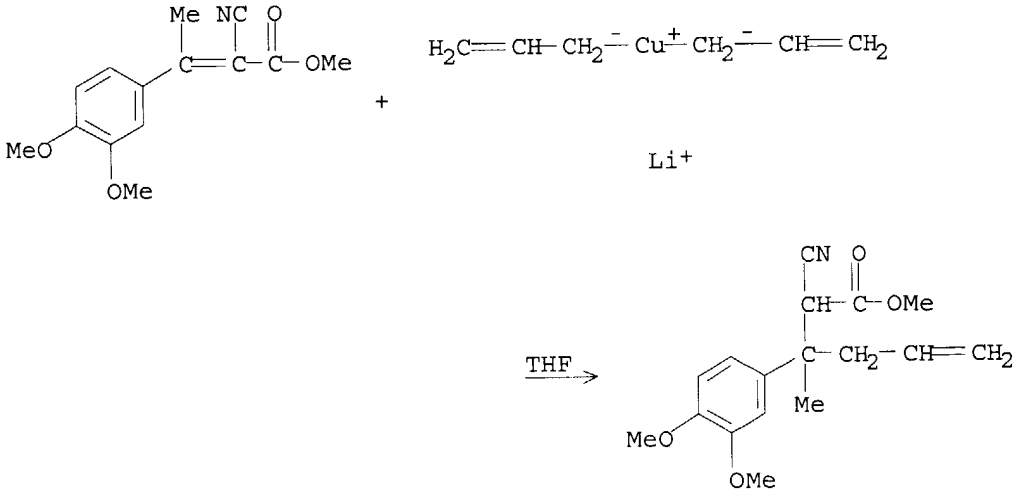
RX(29) OF 57



REF: Journal of Chemical Research, Synopses, (3), 66-7; 1987

L3 ANSWER 6 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

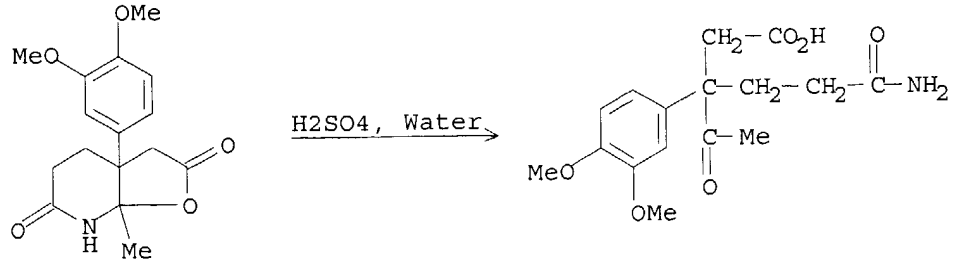
RX(2) OF 45



REF: Heterocycles, 24(7), 1791-3; 1986

L3 ANSWER 7 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

RX(3) OF 258



REF: Journal of Chemical Research, Synopses, (12), 382-3; 1985

L3 ANSWER 8 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

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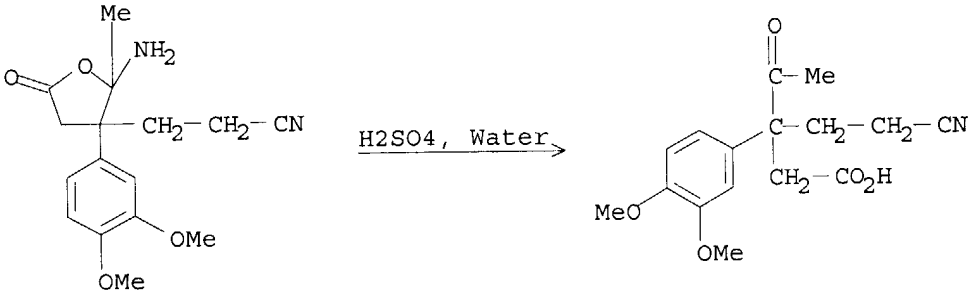

REF: Journal of Chemical Research, Synopses, (4), 112-13; 1985

L3 ANSWER 9 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

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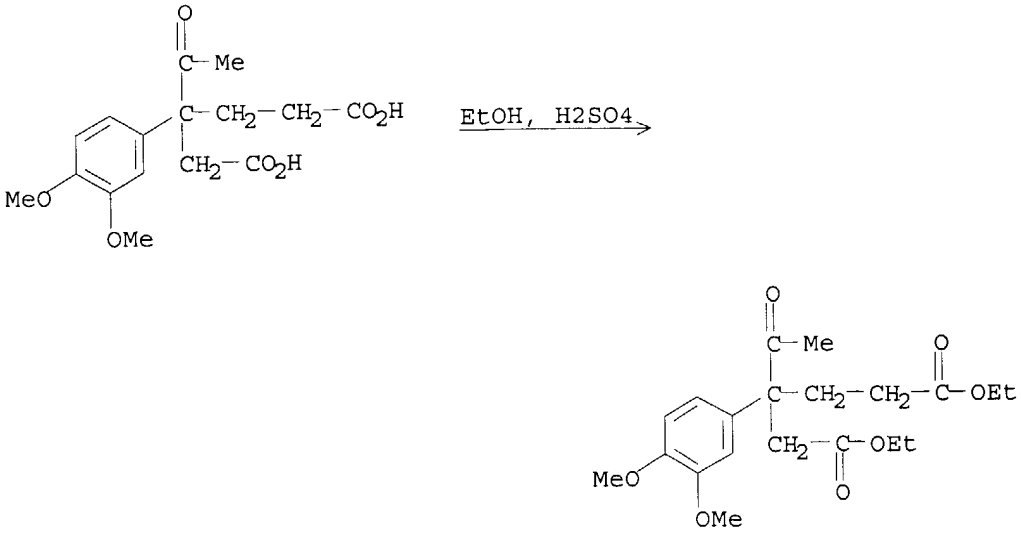

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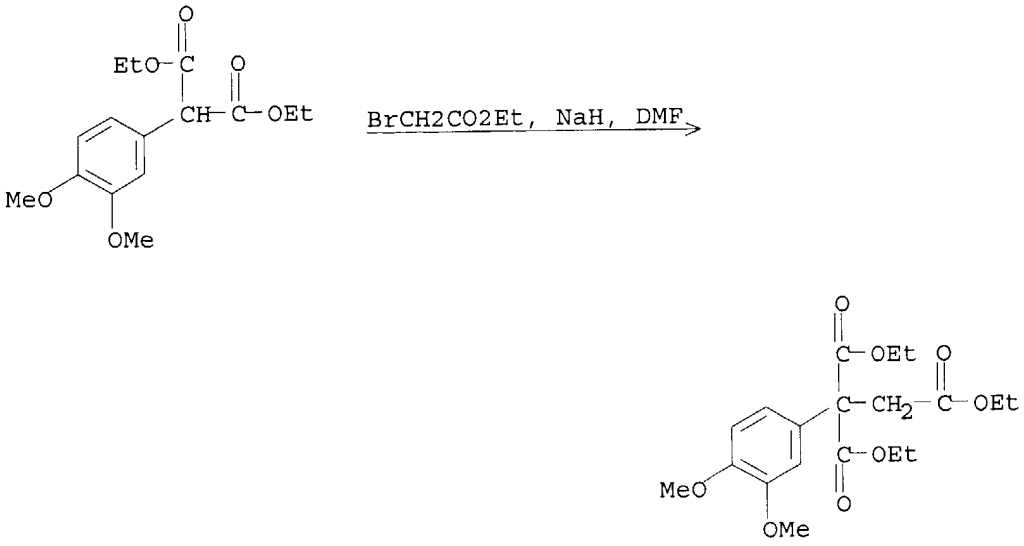
REF: Synthesis, (5), 394-7; 1980

L3 ANSWER 10 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

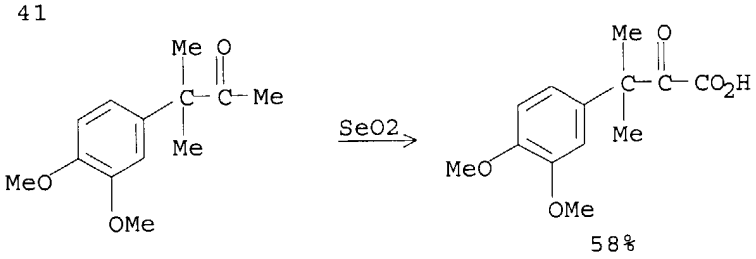
RX(9) OF 26



REF: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999), (11), 1263-5; 1977

L3 ANSWER 11 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

RX(3) OF 41



REF: Acta Pharmaceutica Suecica, 13(1), 65-74; 1976

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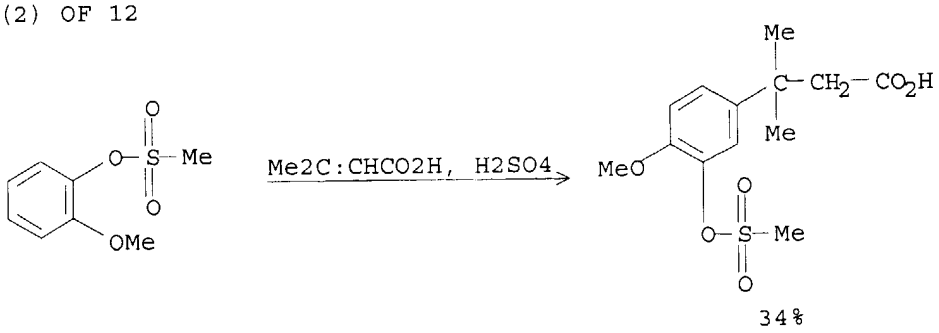
L3 ANSWER 2 OF 11 CASREACT COPYRIGHT 2004 ACS on STN

RX(2) OF 12



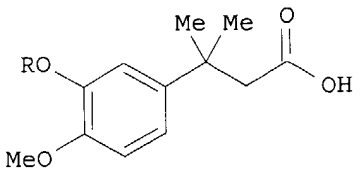
REF: PCT Int. Appl., 2001038297, 31 May 2001
NOTE: 70.degree. for 12 h

=> d l3 bib abs 2
YOU HAVE REQUESTED DATA FROM FILE 'CASREACT' - CONTINUE? (Y)/N:yu
YOU HAVE REQUESTED DATA FROM FILE 'CASREACT' - CONTINUE? (Y)/N:y

L3 ANSWER 2 OF 11 CASREACT COPYRIGHT 2004 ACS on STN
AN 135:5819 CASREACT
TI Preparation of 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyric acid derivative as novel intermediate for sweetener with high sweetness and process for producing the same
IN Kawahara, Shigeru; Mori, Kenichi; Nagashima, Kazutaka; Takemoto, Tadashi
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001038297	A1	20010531	WO 2000-JP7913	20001109
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001013052	A5	20010604	AU 2001-13052	20001109
	EP 1236713	A1	20020904	EP 2000-974890	20001109
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRAI	JP 1999-328100		19991118		
	WO 2000-JP7913		20001109		

OS MARPAT 135:5819
GI



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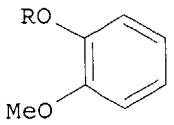

II

AB The title compds. (I; R = sulfonyl-type protecting group) can be obtained by substituting the substituent at the 3-position of the benzene ring of a butyric acid derivative which can be easily and efficiently produced by reacting a hydroxyl-protected 2-methoxyphenol (II; R = same as above), wherein the hydroxyl group of 2-methoxyphenol is protected in the form of a sulfonate, with 3-methylcrotonic acid in the presence of an acid. By further converting the carboxyl group into a formyl group, 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyraldehyde can be easily produced. This aldehyde derivative can be easily derived into a compound, which is excellent as a sweetener with a high sweetness, by reductive alkylation with aspartame. Thus, 104 g AlCl3 was added to a solution of 240 g 2-methanesulfonyloxyanisole and 39 g 3-methylcrotonic acid, stirred at 70° for 5 h and 100° for 2 h, cooled to room temperature, treated with 390 mL 6 N HCl, stirred vigorously for 3 h, and extracted with 300 mL CH2Cl2. The organic layer was extracted with 400 mL 2 N NaOH and the separated aqueous layer was acidified with 6 N HCl, and extracted twice with 300 mL CH2Cl2. The organic layer was concentrated under reduced pressure to give a residue containing 3-(3-methanesulfonyloxy-4-methoxyphenyl)-3-methylbutanoic acid which was treated with 300 mL 6 N NaOH, stirred at 100° for 4 h, cooled to room temperature, acidified with 6 N HCl, and extracted with EtOAc to give, after evaporation of the solvent from the extract and recrystn. from toluene, 37.9% 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutanoic acid (III). III (13.6 g), 22.8 g pivalic acid anhydride, and 100 mL acetone were enclosed in a high pressure hydrogenation apparatus, purged by bubbling N for 30 min, treated with a solution of 137 mg Pd(OAc)2 and 930 mg tri(p-tolyl)phosphine in 5 mL THF, and stirred at 80° under 5 MPa hydrogen pressure to give, after evaporation of acetone and column chromatog., 80% 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyraldehyde (IV). Aspartame (8.45 g) was added to a solution of 6.68 g IV in 272 mL 80% aqueous methanol and the resulting slurry was hydrogenated in the presence of 2.86 g 10% Pd-C (50% water content) at 25° for 24 h, filtered, and the filtrated was treated with 190 mL water and extracted with 250 mL PhMe. The separated methanol-water layer was concentrated under reduced pressure to .apprx.1/2 weight, cooled from 75° to 5°, and filtered to collect the precipitated crystals to give, after crystallization from 50% aqueous MeOH, 67.6% N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-Me ester (98% purity), which is a sweetening agent with high sweetness (no data).

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l17 bib abs

L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:896499 CAPLUS
DN 136:20072
TI 1-Benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivatives and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases

IN Burkholder, Timothy P.; Bratton, Larry D.; Kudlacz, Elizabeth M.; Maynard, George P.; Kane, John M.; Santiago, Braulio

PA Aventis Pharmaceuticals, Inc., USA

SO U.S., 77 pp., Cont.-in-part of U.S. Ser. No. 501,914, abandoned.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6329392	B1	20011211	US 1998-79924	19980515
	CA 2198084	AA	19960229	CA 1995-2198084	19950817
	CN 1158612	A	19970903	CN 1995-195283	19950817
	CN 1067385	B	20010620		
	HU 76644	A2	19971028	HU 1997-1257	19950817
	HU 221434	B	20021028		
	AT 177095	E	19990315	AT 1995-931551	19950817
	ES 2132709	T3	19990816	ES 1995-931551	19950817
	ZA 9507033	A	19960416	ZA 1995-7033	19950822
	IL 115040	A1	20000229	IL 1995-115040	19950823
	TW 430663	B	20010421	TW 1995-84108797	19950823
PRAI	US 1994-295960	B2	19940825		
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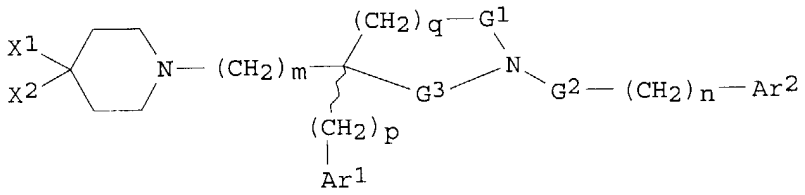
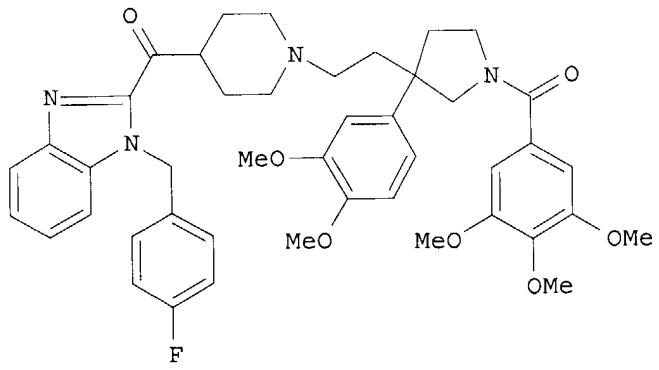
OS MARPAT 136:20072

GI



I



II

AB The present invention relates to novel substituted piperidine derivs. I wherein: G1 is CH2 or CO; G2 is CH2 or CO; G3 is CH2 or CO; m is 2 or 3; n is 0 or 1; q is 1 or 2; p is 0 or 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, pyridyl; X1 and X2 are defined in one of (A), (B), or (C): (A) X1 = H and X2 = substituted benzothiazole-2-carbonyl, diphenylmethyl, benzimidazolyl-2-carbonyl; (B) X1 = OH and X2 = substituted benzothiazol-2-yl, benzimidazol-2-yl; (C) X2 = (R5C6H4)C(Z1)(C6H4R6) wherein R5, R6 = from 1 to 3 substituents chosen independently from, e.g., H, halo, CF3, and X1 and Z1 taken together form a second bond between the carbon atoms bearing X1 and Z1; provided than when G1 is CO, then G2 and G3 are CH2, and that when G2 is CO, then G1 and G3 are CH2, and that when G3 is CO, then G1 and G2 are CH2; stereoisomers thereof, and pharmaceutically acceptable salts thereof which are useful as

histamine receptor antagonists and tachykinin receptor antagonists. Such antagonists are useful in the treatment of allergic diseases including: seasonal rhinitis, allergic rhinitis, and sinusitis. Thus, e.g., substitution reaction of 4-[1-(4-fluorobenzyl)-1H-benzimidazole-2-carbonyl]piperidine with 1-(3,4,5-trimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine (preparation given) afforded II which exhibited H1 receptor antagonism in vitro with pA2 = 7.50, and NK1 receptor binding affinity with IC50 = 31 nM.

RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 10:31:10 ON 30 JUN 2004)

FILE 'CASREACT' ENTERED AT 10:31:21 ON 30 JUN 2004
L1 STRUCTURE UPLOADED
L2 0 S L1 SSS
L3 11 S L1 SSS FULL
L4 0 S L1

FILE 'CAPLUS' ENTERED AT 10:34:10 ON 30 JUN 2004
L5 11 S L3

FILE 'REGISTRY' ENTERED AT 10:34:19 ON 30 JUN 2004
L6 1 S 541-47-9/RN

FILE 'CAPLUS' ENTERED AT 10:34:48 ON 30 JUN 2004
L7 983 S L6
L8 1 S L7 AND L5

FILE 'REGISTRY' ENTERED AT 10:37:12 ON 30 JUN 2004

FILE 'CAPLUS' ENTERED AT 10:37:12 ON 30 JUN 2004

FILE 'REGISTRY' ENTERED AT 10:38:13 ON 30 JUN 2004
L9 STRUCTURE UPLOADED
L10 1 S L9 SSS
L11 48 S L9 SSS FULL
L12 STRUCTURE UPLOADED
L13 50 S L12 SSS
L14 281769 S L12 SSS FULL

FILE 'CAPLUS' ENTERED AT 10:39:51 ON 30 JUN 2004
L15 0 S L11 AND L14 AND L6
L16 33 S L11/PREP
L17 1 S L16 AND L14
L18 0 S L17 AND L6

FILE 'REGISTRY' ENTERED AT 10:46:32 ON 30 JUN 2004

FILE 'CAPLUS' ENTERED AT 10:46:33 ON 30 JUN 2004

FILE 'CASREACT' ENTERED AT 10:47:17 ON 30 JUN 2004

FILE 'CAPLUS' ENTERED AT 10:47:21 ON 30 JUN 2004

FILE 'CASREACT' ENTERED AT 10:50:58 ON 30 JUN 2004

FILE 'CAPLUS' ENTERED AT 10:51:02 ON 30 JUN 2004

FILE 'REGISTRY' ENTERED AT 10:55:38 ON 30 JUN 2004

FILE 'CAPLUS' ENTERED AT 10:55:38 ON 30 JUN 2004

FILE 'CASREACT' ENTERED AT 11:00:23 ON 30 JUN 2004

FILE 'CAPLUS' ENTERED AT 11:00:26 ON 30 JUN 2004

FILE 'CASREACT' ENTERED AT 11:04:11 ON 30 JUN 2004

FILE 'CAPLUS' ENTERED AT 11:04:11 ON 30 JUN 2004

FILE 'CASREACT' ENTERED AT 11:04:23 ON 30 JUN 2004

FILE 'CAPLUS' ENTERED AT 11:04:23 ON 30 JUN 2004

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